C-arm CT Perfusion Study Using Angiography System

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Objective: A newly developed application for cerebral C-arm computed tomography perfusion imaging (C-arm CTP) using an angiography system was investigated.

Case Presentation: C-arm CTP protocol continuously collects X-ray projection images during 10 back and forth C-arm rotations. From the collected data, cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time to peak (TTP) images and multiphase vascular images are reconstructed. C-arm CTP images acquired in patients with acute and chronic major artery occlusion are presented.

Conclusion: C-arm CTP using an angiography system is capable of evaluating perfusion parameters in real time, similar to conventional evaluation using multi-detector row CT perfusion (MD-CTP), suggesting its usefulness for examination of ischemic stroke in the angiographic suite.

Keywords: C-arm computed tomography, computed tomography perfusion, computed tomography angiography, angiography, stroke imaging

Introduction

Through the introduction of a novel software application on a conventional flat panel C-arm angiographic system, the system becomes capable of collecting X-ray projection images during continuous back and forth C-arm rotations. Such time-course collection of image information was previously not possible. Through this improvement, analysis of cerebral perfusion parameters, such as cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time to peak (TTP) became possible (dynamic C-arm computed tomography perfusion [C-arm CTP]).

Currently, these perfusion parameters cannot be evaluated with conventional angiographic systems. Methods currently used to measure cerebral perfusion parameters in clinical practice include single photon emission computed tomography (SPECT), positron emission tomography (PET), and perfusion imaging using MRI and CT. The real-time evaluation of cerebral perfusion parameters during angiography is difficult because methods used for cerebral perfusion imaging are performed in rooms exclusive for these types of modalities. If cerebral perfusion parameters can be analyzed using an angiography system, not only morphological but also functional evaluation can be performed during an endovascular procedure, such as angiography and thrombectomy, without transferring the patient to a different room. C-arm CBV has been reported as a practical method to evaluate cerebral perfusion parameters using an angiography system. C-arm CBV is acquired at steady state of contrast medium flow in brain tissue. Since acquired information is limited to CBV, this method is useful to detect cerebral infarction, as a region with reduced CBV reflecting cerebrovascular occlusion-induced blockage of blood flow. However, the information in a CBV image is insufficient to evaluate mismatch between the area perfused by the occluded vessel and the salvageable ischemic area. If cerebral circulation parameters, such as CBF, CBV, and MTT, can be calculated using C-arm CTP, evaluation of these images in the angiography...
suite can be performed in a similar way to evaluate CTP (multi-detector row CT perfusion; MD-CTP) using widely used multi-detector CT (MD-CT). Shortening the time to recanalization of the occluded vessel is a major proposition of current treatment of cerebral infarction. If the patient’s condition can be evaluated in an angiographic suite immediately after arrival to the hospital, it is a great advantage in shortening the time to recanalization. C-arm CTP is still under development and its clinical application including the acquisition method has just started. Thus, in this study, we report the acquisition method, current problems, and future possibility of C-arm CTP performed using a newly developed prototype application.

### Case Presentation

#### Methods

C-arm CTP was performed after approval by the Ethics Committee of our hospital. The examination was sufficiently explained to the patients and their families at the time of explaining cerebral angiography and endovascular treatment and consent was obtained.

For C-arm CTP, a biplane flat-panel angiography system (Artis zee biplane, Siemens Healthcare GmbH, Forchheim, Germany) usually used at our hospital for diagnosis and treatment can be used as is. For control of C-arm rotation and image information analysis, a workstation equipped with the prototype C-arm CTP analysis program was used.

#### Acquisition method and image analysis of C-arm CTP

The data acquisition protocol and image analysis of C-arm CTP are shown in Fig. 1. Information was continuously acquired during 10 back and forth C-arm rotations. Since contrast medium injection started 5 seconds after initiation of the scan, the first two acquisitions served as the baseline non-enhanced (mask) images, and the subsequent eight acquisitions were enhanced (fill) images in which intravascular circulation of the contrast medium was detected. The protocol uses a 0.3-second pause between each two subsequent C-arm rotations. Each C-arm rotation covers 200° angle in 5 seconds and results in 248 2D X-ray projections (angulation step: 0.80/frame). The tube voltage was 77 kVp,
detector entrance dosage, 0.36 μGy/frame; and total acquisition time, 61.3 seconds.

Contrast medium injection protocol is similar to that used in MD-CTP. A 20-G needle was inserted into the left cubital vein as a contrast route. Using a dual syringe power injector (Press Duo, Nemoto Kyorindo Co., Ltd., Tokyo, Japan), 40 mL of 300 mgI/mL non-ionic iodine contrast medium (Oypalomin, Fuji Pharma Co., Ltd., Toyama, Japan) was injected at a speed of 4 mL/sec, followed by flushing of 30 mL of saline at the same speed.

Acquisition datasets were analyzed using prototype perfusion software. Currently, it takes about 5 minutes to prepare perfusion images after completion of acquisition because the acquired data are sent to the prototype workstation, reconstructed, and then analyzed. C-arm CTP perfusion images are automatically analyzed based on the deconvolution method. The details of the analysis application are not disclosed, but the theory of the analysis has been previously reported.\(^1\)\(^-\)\(^3\) Control of C-arm rotation and analysis of the collected data were limited at the beginning of development and slightly different from the method used in this study. However, the concept of the acquisition and analytical methods was not changed, and improvement has been continuously made to increase the accuracy of analysis of collected data. Since in C-arm CTP, information is collected from the entire brain by the flat panel, a perfusion image with a desired slice orientation and slice thickness can be prepared from the collected image information. To easily compare with other perfusion modalities, we prepared CBF, CBV, MTT, and TTP maps using 5-mm thick axial sections. In addition, images of vascular structures in each acquisition phase can be simultaneously reconstructed based on the 2D projection images acquired during a single rotation of C-arm CTP protocol. Thus, using the maximum intensity projection (MIP) image, we confirm continuous intravascular changes from the early phase to after passage of contrast medium and use these to confirm the occluded region and presence or absence of collateral circulation in patients with acute major cerebral artery occlusion.

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**Fig. 2** Case 1, a 62-year-old male with chronic right cervical ICA occlusion. (A) Axial T2-weighted MRI showed old infarcted scars at the right frontal and parietal regions. (B) MR angiography showed remarkable decrease in the vascular signal in the right ICA. (C) A cervical lateral view of the right CCAG. Occlusion at the bifurcation of the right cervical ICA was observed. (D) An antero-posterior view of the left CCAG showed right ICA occlusion and collateral flow via the anterior communicating artery. (E–G) C-arm CT perfusion map revealed remarkable reduced CBF (E) and slightly increased CBV (F) in the right MCA territory, as opposed to the left hemisphere. The extent of the ischemic lesions is clearly identified on the MTT map (G). \(^{123}\)I-IMP-SPECT showed significant reduced CBF as the same area with the C-arm CTP CBF map (H). CBF: cerebral blood flow; CBV: cerebral blood volume; CCAG: common carotid artery angiogram; CTP: computed tomography perfusion; ICA: internal carotid artery; MCA: middle cerebral artery; MTT: mean transit time; SPECT: single photon emission computed tomography; \(^{123}\)I-IMP: N-isopropyl-p-[\(^{123}\)I]iodoamphetamine
Presentation of Representative Cases

Case 1
A 62-year-old male with chronic right cervical internal carotid artery occlusion. He had a past medical history of motor weakness and sensory disturbance of the left side and visited our hospital for close examination. Old cerebral infarctions were noted in the right frontal and parietal lobes on MRI, and right internal carotid artery occlusion was detected on MRA (Fig. 2A and 2B). On cerebral angiography, the right internal carotid artery was occluded in the cervical region, and the right cerebral hemisphere was perfused by cross flow via the anterior communicating artery (Fig. 2C and 2D). On C-arm CTP, reduction of CBF and a slight increase in CBV were detected in the right middle cerebral artery territory (Fig. 2E and 2F), and MTT was markedly extended (Fig. 2G). On N-isopropyl-p-[123I] iodoamphetamine (123I-IMP)-SPECT at rest performed at the same time at the outpatient clinic, reduction of blood flow in the right middle cerebral artery region similar to that observed in the CBF image acquired on C-arm CTP was confirmed (Fig. 2H). Hemodynamic cerebral ischemia was suspected, but at present, the patient is asymptomatic and does not want surgical treatment. Thus, the course is followed with antiplatelet drug treatment alone.

Case 2
An 80-year-old female. The disease manifested with consciousness disturbance and left hemiplegia (National Institutes of Health Stroke Scale [NIHSS] 20). A high intensity was noted in the right putamen and corona radiata on diffusion-weighted image (DWI) of MRI performed at the time of arrival (Fig. 3A and 3E), and occlusion was detected in the distal right internal carotid artery on MRA. Moreover, atrial fibrillation was detected on electrocardiography on arrival. The accurate onset time was unclear, but the ischemic region on DWI was relatively localized and inconsistent with the severity of consciousness disturbance and neurologic findings. Thus, the patient was immediately transferred to an angiographic suite. First, C-arm CTP was performed. Extension of MTT was confirmed extensively in the right cerebral hemisphere, but the region with reduced CBF and CBV remained in the ischemic area observed on DWI (Fig. 3B–3D and 3F–3H). In time-course vascular images prepared at the same time, the occluded region of the
right internal carotid artery (Fig. 4B, arrow) and the distal side of the occluded region visualized through collateral circulation were confirmed (Fig. 4A–4C). Considering that an ischemic region which can be salvaged by reperfusion is present, thrombectomy was immediately performed. On imaging of the right internal carotid artery before treatment, the right internal carotid artery was occluded in the region distal to the ophthalmic artery. Complete recanalization was achieved by the first session of sentriever deployment (Fig. 4D–4G) and neurologic manifestation markedly improved after recanalization (NIHSS 3). On postoperative C-arm CTP, the region with noticeable extension observed on the MTT map before treatment markedly improved, and no new region with reduction was noted in the CBF or CBV map (Fig. 5A–5C and 5E–5G). On MRI on the day following treatment, cerebral infarction was completed being consistent with the high-intensity region on DWI on arrival, but no expansion of infarction was observed in any other region (Fig. 5D and 5H). Oral anticoagulant treatment was initiated and the patient was discharged to home at modified Rankin Scale 1 14 days after admission.

### Discussion

In CT perfusion imaging, CT images are continuously acquired during the first cerebral circulation after non-ionic iodine contrast medium injection as an intravascular tracer. Changes in the CT value in brain tissue are measured, and cerebral circulation parameters including CBF, CBV, and MTT are determined from the time–attenuation curve. In one of the first attempts to collect information on cerebral perfusion using this CT, Axcel reported the measurement theory as a dynamic CT method in 1980. As slin ring-type CT capable of rapidly acquiring images appeared later, Koenig et al. reported clinical application as perfusion CT. Since then, perfusion CT has become widely used in clinical practice because of the rapidness and simplicity applicable to patients with acute cerebral ischemia, and the capability of collecting decision-making information to indicate treatment and predict the outcome. On the other hand, for imaging of the cerebral circulation using an angiography system, C-arm CBV images which reflect steady-state contrast medium distribution in
brain tissue has been mainly reported.\(^4\)\(^-\)\(^9\) In addition, improvement of the angiography system and data acquisition methods has recently been tried and experimental studies on C-arm CTP described in this study have been occasionally reported.\(^1\)\(^-\)\(^3\),\(^10\)\(^-\)\(^19\)

**Figure 6** outlines the three approaches for cerebral perfusion imaging using contrast medium performed at our institution. For C-arm CBV, the imaging protocol time is short (24 seconds) because images are acquired after an appropriate scan delay time to achieve steady state of contrast medium in brain tissue. Both C-arm CTP and MD-CTP imaging protocols require about 60 seconds because, in each method, changes in the first circulation in the brain after contrast medium injection are imaged over time to yield a time–attenuation curve. Therefore, an injection protocol for C-arm CTP was prepared using the same contrast medium injection method employed in MD-CTP. C-arm CTP is inherently limited by the rotation speed of the C-arm and by the change in the C-arm rotation direction between each two subsequent C-arm rotations. In MD-CTP, since CT images can be acquired while the detector is rotating at a high speed, changes in the CT value in the first circulation of the administered contrast medium in the cranium can be finely detected, and the number of measurement points during the examination is 38. On the other hand, in C-arm CTP, C-arm rotation in one direction takes 5 seconds and the first two acquisitions are used as mask images. Thus, at present, the number of measurement points used for the time–attenuation curve is 8. Although the details of the analysis program of the perfusion imaging analysis software are not disclosed, the time–attenuation curve is prepared by utilizing fewer CT value data points, and various perfusion parameters are calculated from it. Wintermark et al. investigated the influences of the amount of contrast medium and information sampling interval on CT perfusion imaging using MD-CT. They stated that the area under the time–attenuation curve is overestimated as the number of data samples decreases, that is, when the information sampling interval is wide and the number of samples is small, CBV is overestimated and MTT is underestimated, resulting in the overestimation of CBF.\(^20\) Royalty et al. compared CBF and CBV measurements between C-arm CTP and MD-CTP and observed that CBF and CBV measured on C-arm CT were overestimated compared with those on MD-CTP in quantitative analysis.\(^3\) However, in qualitative evaluation to mainly identify the area with abnormal

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**Fig. 5** Case 2, an 80-year-old female with acute ischemic stroke. C-arm CT perfusion maps just after thrombectomy (A–C and E–G). CBF and CBV maps demonstrated slightly increased regional CBF (A and E) and CBV (B and F) in the right putamen and corona radiata. A significant improvement of cerebral perfusion was recognized at the right ICA territory on the MTT maps (C and G). DWI 24 hours after treatment showed early ischemic change in the right putamen and corona radiata. However, no other ischemic change was observed in the right cerebral hemisphere (D and H). CBF: cerebral blood flow; CBV: cerebral blood volume; ICA: internal cerebral artery; MTT: mean transit time; DWI: diffusion weighted image.
Another characteristic of C-arm CTP is that vascular information can be acquired. Vascular images can be prepared within about 3 minutes using the prototype workstation, in addition to preparation of perfusion images. Yang et al. reported that the ability to visualize the major arteries in images prepared from C-arm CTP and to make a diagnosis is sufficient.19) We confirmed the region with vascular occlusion as a visualization defect between the proximal side with disruption of visualization and distal side visualized through collateral circulation, as shown in Case 2. This suggests that when thrombectomy is considered, the procedure can be applied based on the identified location of the region with vascular occlusion in addition to the information on the distal side of the occluded region visualized through collateral circulation.

Regarding the prospects of C-arm CTP using an angiography system, the “one-stop-shop” concept has been proposed.10,13,19) Under this concept, when a patient suspected of having stroke visits a hospital, the patient is
immediately transferred to an angiographic suite and morphological examination is performed by C-arm CT followed by C-arm CTP to evaluate cerebral perfusion parameters and vascular structures. This concept aims at shortening the time to treatment by reducing time lost due to transfer of the patient between different rooms and examination by other examination modalities. Images acquired by CT and MRI are snapshots at the time of examination, and when there is a time interval to the initiation of actual treatment, the condition may be different from that at the time of the initial examination. Therefore, the concept to evaluate the condition immediately before treatment initiation is very useful. One concern with C-arm CTP is that the volume of contrast medium used for single examination is 40 mL in addition to the contrast volume used in cerebral angiography and endovascular treatment. Moreover, an increase in the radiation exposure dose is of concern. Yang et al. stated that the total exposure dose of 9 C-arm rotations during C-arm CTP acquisition was 4.6 mGy, whereas that of normal MD-CTP was 5.0 mGy. Struffert et al. reported that additional 3–5 mGy exposure dose is necessary when MD-CTA is performed simultaneously with MD-CTP. In the current acquisition method presented in this study, the total exposure dose was 5.1 mGy because the protocol used involves one additional C-arm rotation compared to the protocol in reported studies. However, this exposure dose is almost the same as that in MD-CTP. Considering that rich information, such as CBF, CBV, and MTT, are acquired by C-arm CTP, and that vascular information including occlusions and collateral circulation can be simultaneously acquired, the usefulness of this method may exceed the disadvantages of the increase in the contrast medium volume and exposure dose. Despite the concerns with the current implementation of C-arm CTP, it may sufficiently contribute to the evaluation of the state of acute cerebral ischemia and to shortening the time to recanalization via mechanical thrombectomy.

### Conclusion

Similar to conventional MD-CTP, C-arm CTP using an angiography device is capable of evaluating cerebral circulation. In addition, cerebral perfusion parameters can be measured and vascular anatomy can be evaluated in real time in the angiographic suite, suggesting that C-arm CTP is a useful tool to help diagnose stroke and judge the effect of treatment.

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### Disclosure Statement

This study was performed using workstation equipped with the prototype C-arm CTP analysis program provided by Siemens Japan K.K. There is no other conflict of interest for the first author and coauthors related to this work.

### References


